

From the  
INTERNATIONAL SEARCHING AUTHORITY

PATENT COOPERATION TREATY

REC'D 07 MAR 2005

PCT/WIPO

PCT

To:  
GEOFFREY L. MELNICK  
G.E. EHRLICH (1995) LTD.  
11 MENACHEM BEGIN STREET  
RAMAT GAN, ISRAEL 52 521

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

|  |   |   |
|--|---|---|
| Applicant's or agent's file reference<br>28210   |   | Date of mailing<br>(day/month/year)<br>02 MAR 2005          |
| International application No.<br>PCT/IL04/00661  | International filing date (day/month/year)<br>20 July 2004 (20.07.2004) | Priority date (day/month/year)<br>21 July 2003 (21.07.2003) |
| International Patent Classification (IPC) or both national classification and IPC<br>IPC(7): C12M 3/00; C12N 5/00 and US Cl.: 435/395, 305.2 |   |   |
| Applicant<br>MOLECULAR CYTOMICS LTD.   |   |   |

1. This opinion contains indications relating to the following items:

|                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

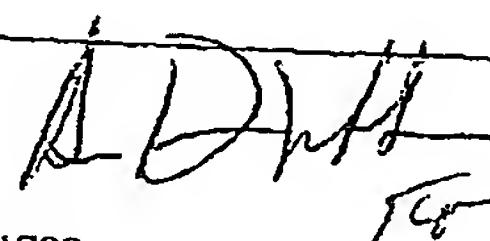
Name and mailing address of the ISA/ US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (703) 305-3230

Form PCT/ISA/237 (cover sheet) (January 2004)

Authorized officer

William H. Beisner

Telephone No. 571-272-1700



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/IL04/00661

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

a sequence listing

table(s) related to the sequence listing

b. format of material

in written format

in computer readable form

c. time of filing/furnishing

contained in international application as filed.

filed together with the international application in computer readable form.

furnished subsequently to this Authority for the purposes of search.

3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/IL04/00661

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

|                               |  |     |
|-------------------------------|--|-----|
| Novelty (N)                   | Claims <u>2,3,5-7,39,40,49,53,55-81,88-185</u> | YES |
|                               | Claims <u>1,4,8-38,41-48,50-52,54,82-87</u>    | NO  |
| Inventive step (IS)           | Claims <u>NONE</u>                             | YES |
|                               | Claims <u>1-185</u>                            | NO  |
| Industrial applicability (IA) | Claims <u>1-185</u>                            | YES |
|                               | Claims <u>NONE</u>                             | NO  |

2. Citations and explanations:

Claims 1, 4, 8-38, 41-48, 50-52, 54 and 82-87 lack novelty under PCT Article 33(2) as being anticipated by Deutsch et al. With respect to claim 1, the reference of Deutsch et al. discloses a multiwell plate that includes a plurality of wells defined by walls (40) (See Figure 52) wherein each well includes a plurality of picowells. With respect to claim 4, the wells are rectangularly packed. With respect to claims 8-38, see Figures 1-26 and related disclosure. With respect to claims 41-48, 50-52 and 54, see page 37, first full paragraph, which discloses the materials and laminated structure of the device. With respect to claims 82-87, see Figure 26 and related disclosure that discusses the use of micromachined elements for adding, removing and/or detecting relative to the cells within the picowells.

Claims 2, 3, 5-7, 39, 40, 49, 53, 66-80, 88-106 and 113-134 lack an inventive step under PCT Article 33(3) as being obvious over Deutsch et al. The reference of Deutsch et al. has been discussed above. With respect to claims 2, 3 and 5-7, while the reference does not specifically disclose the use of a 96 well format, it would have been obvious to one of ordinary skill in the art to employ a 96 well format for the known and expected result of providing a standardized well format that is compatible with the industry standard for automation of well plates. With respect to claims 39, 40, 49, 53, 66-69 and 73-78, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum material of construction based on design considerations such as the size of the picowells and intended use of the device while maintaining the intended function of the device. With respect to claims 70-72, 79 and 80, the use of coatings within culture wells is known in the art and would have been obvious for the known and expected results of controlling the adhesion of desirable cells and/or preventing the adhesion of undesirable cells. With respect to claims 88-134, based merely on the specific material of construction, it would have been obvious to one of ordinary skill in the art to select a method of manufacture which is associated with the specific material of manufacture so as to optimize the construction of the device.

Claims 55-65, 81, 107-112 and 135-185 lack an inventive step under PCT Article 33(3) as being obvious over Deutsch et al. in view of Hammerick et al., Bochner et al. and Leighton et al. The reference of Deutsch et al. has been discussed above. The reference of Hammerick et al. discloses a cell holding device for individually supporting cells wherein the material of construction can be a hydrogel material (See paragraph [0083]). The reference of Bochner et al. discloses that the use of a gel material or cover with a microplate device is known in the art to avoid contamination (See column 8, lines 44-56). The reference of Leighton et al. also discloses that it is known in the art to encapsulate a culture of cells from the environment using a gel membrane (See column 3, line 54, to column 4, line 5). In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the primary reference with a gel matrix or cover for the known and expected result of providing a means recognized in the art for maintaining a cell culture in a sealed configuration while protecting the cells from a surrounding environment that can be contaminated by the cells or the cells contaminated by the surrounding environment.

Claims 1-185 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.